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S. 3187 – The Food and Drug Administration Safety and Innovation Act

On April 25, 2012, the Senate Health, Education, Labor and Pensions (HELP) Committee reported S. 2516, a five year FDA user fee reauthorization bill, by voice vote. On May 15, HELP Committee Chairman Harkin and Ranking Member Enzi filed an updated bill, S. 3187. This new bill includes the full text of S. 2516, as reported by the HELP Committee, and a bipartisan managers' package. Majority Leader Reid placed S. 3187 on the Senate Calendar on May 16, 2012.

Noteworthy

- S. 3187 reauthorizes for five years user fee programs for prescription drugs and medical devices.
- The bill also establishes new user fee programs for generic drugs and biosimilars.
- S. 3187 further contains Food and Drug Administration (FDA) reforms.
- Current prescription drug and medical device user fee agreements expire on September 30, 2012.
- If Congress does not authorize new user fee agreements, the FDA must lay off staff which would disrupt FDA's pre-market review programs.

Background

On April 25, 2012, the Senate Health, Education, Labor and Pensions (HELP) Committee voice voted to report a bipartisan five-year FDA user fee reauthorization bill to the full Senate for its consideration. The bill was placed on the Senate Calendar on May 7, 2012. The legislation is titled "The Food and Drug Administration Safety and Innovation Act."

On May 8, 2012, the House Energy and Commerce's Subcommittee on Health considered a similar, but not identical, measure. The health subcommittee unanimously reported an FDA user fee bill to the full committee by voice vote. On May 10, 2012, the Committee unanimously approved H.R. 5651, the "Food and Drug Administration Reform Act", by a vote of 46 to 0.

Bill Provisions

Title I – Fees Relating to Drugs

This title reauthorizes the Prescription Drug User Fee Act, commonly called PDUFA V. It authorizes the Secretary of Health and Human Services (HHS) to continue collecting fees from the pharmaceutical industry to support the FDA's human drug application review process.

Specifically, this title continues three types of industry fees: application fees; establishment fees; and product fees. An application fee is assessed each time a sponsor submits an application for product approval. An establishment fee is assessed for each facility that manufactures prescription drugs or devices. A product fee is assessed for each product on the market.

This title sets total PDUFA fee revenue in fiscal year 2013 at $693 million. It modifies the formula used to calculate annual fee inflation adjustments to reflect FDA personnel and benefit costs.

The PDUFA V user fee authority would sunset on October 1, 2017.

Title II – Fees Relating to Devices

This title reauthorizes the Medical Device User Fee Act, commonly called MDUFA III. The new MDUFA agreement allows the Secretary of HHS to collect $595 million in fees from the medical device industry over a five year period (fiscal years 2013 – 2017).

This title also requires: (1) the FDA to report total time to review devices; (2) the FDA offer greater sponsor interaction during a review process; and (3) an independent entity review of the device approval and clearance process so that the FDA can implement a corrective action plan if any deficiencies are found.

The MDUFA III user fee authority would sunset on October 1, 2017.

Title III – Fees Relating to Generic Drugs

This title authorizes a new Generic Drug User Fee Act (GDUFA). The proposed generic drug user fee provides additional resources to review and regulate generic pharmaceuticals. This title authorizes the Secretary of HHS to collect approximately $299 million each year from fiscal years 2013 through 2017. The generic drug industry agreed to this fee in return for FDA support to eliminate application backlogs and ensure that foreign generic manufacturers are subject to appropriate regulatory scrutiny.

The GDUFA user fee authority would sunset on October 1, 2017.

Title IV – Fees Relating to Biosimilar Biological Products

This title authorizes a new Biosimilars User Fee Act (BsUFA). This user fee targets products approved, under the abbreviated approval pathway, that are shown to be biosimilar to an FDA-licensed biological product.

The BsUFA creates six different types of new industry fees: (1) initial product development fee; (2) annual product development fee; (3) reactivation fee; (4) product application fee; (5) product establishment fee; and (6) product fee. Each fee calculation is based on inflation-adjusted PDUFA fee amounts in each fiscal year.

Finally, this title requires that the Secretary of HHS waive the biosimilar biological product application fee submitted by a small business. A small business is defined as an entity that employs fewer than 500 workers and does not have: (1) a drug product that has been approved under a human drug or biosimilar biological application; and (2) a drug product that has been introduced or delivered into the marketplace.

The BsUFA user fee authority would sunset on October 1, 2017.

Title V – Pediatric Drugs and Devices

Section 501

This section permanently authorizes the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA). BPCA provides additional exclusivity for pharmaceutical companies that study their drug in children for a different use than the labeled indication (if that use is ethical and applicable). BPCA works with PREA for the development of prescription drugs for children.

Section 502

This section clarifies the FDA's authority to grant longer marketing exclusivity periods to drug manufacturers in return for FDA-requested pediatric use studies and reports.

Section 503

This section requires the Secretary of HHS to issue guidance allowing Pediatric Review Committee evaluation of significant modifications to written requests or pediatric study plans.

Section 504

This section instructs the Secretary of HHS to make public, no later than three years after enactment, the medical, statistical, and clinical pharmacology reviews of written requests made between 2002 and 2007.

Section 505

This section allows pediatric study deadline extensions in appropriate circumstances. Current tracking requirements are expanded to collect data about deferral extensions as well as the timeline to complete assessments. If a required pediatric study is not completed or deferred, then the Secretary of HHS must send a letter requiring a response within 45 days. Communications must be made publicly available.

Section 506

This section ties submission of an initial pediatric study plan to the sponsor's end of phase 2 meeting with the FDA – unless the Secretary of HHS and the applicant agree on another date. Further, the pediatric study plan submissions process is clarified through regulation.

Section 507

This section reauthorizes the Pediatric Advisory Committee and the Pediatric Subcommittee of the Oncologic Drug Advisory Committee, the Humanitarian Device Exemptions Extension, the Demonstration Grants to Improve Pediatric Device Availability, and the Program for Pediatric Study of Drugs.

Section 508

This section requires a report every five years evaluating both the BPCA's and the PREA's effectiveness.

Section 509

This section makes technical corrections to the statute.

Section 510

This section clarifies that labeling changes – made due to a study that was either inconclusive or that failed to demonstrate product safety and effectiveness – do not qualify for three year statutory exclusivity.

Section 511

This section mandates that the Secretary of HHS, no later than 18 months after the date of enactment, conduct a public meeting that brings stakeholders and the FDA together to discuss ways to encourage and accelerate pediatric rare disease therapies. The Secretary must also, within 180 days of conducting the public meeting, issue a report outlining a strategic plan to encourage and accelerate pediatric rare disease therapies and treatments.

Title VI – Medical Device Regulatory Improvements

Section 601

This section allows the FDA to change a device classification through an administrative order rather than by regulation. Authority to issue an administrative order cannot be delegated below the FDA Commissioner, who must consult with the Secretary of HHS.

Section 602

This section codifies the Secretary of HHS' authority to require post-market device studies as a condition of pre-market approval.

Section 603

This section clarifies the Secretary of HHS' authority to order Class II and Class III device post-market surveillance. The order can be made either at the time of approval, at clearance, or at a later time.

Section 604

This section requires the Secretary of HHS include medical devices in its "Sentinel" post-market risk identification and evaluation system. When implementing this change, HHS must engage with stakeholders.

Section 605

This section mandates the Secretary of HHS create a new program assessing submitted or reported medical device recall, removal, and corrections information. The agency can use this information to identify strategies that mitigate health risks from defective or unsafe devices.

Section 606

This section allows the Secretary of HHS to issue a clinical hold. This hold prohibits medical device sponsors from continuing clinical investigations of a device representing an unreasonable risk to patient safety. A device sponsor can request HHS remove a clinical hold. The sponsor must receive a decision, in writing, within 30 days.

Section 607

This section instructs the Secretary of HHS to issue proposed regulations establishing a unique device identification system. The regulations must be made public no later than December 31, 2012, and a final regulation must be issued six months after the comment period closes.

Section 608

This section clarifies the statutory "least burdensome" standard. It forbids the FDA from asking for more than the "minimum required amount" of clinical data.

Section 609

This section clarifies the FDA policy regarding device customization for small (five or fewer per year), unique patient populations. If a device is not available in the U.S., and no other domestic device can treat the patient, then it is not forced to comply with pre-market approval requirements. This applies only if the device is intended to meet a specific, special need of a physician and if the product is custom made to meet an individual's unique physiology.

Section 610

This section mandates the Secretary of HHS provide a written summary outlining the agency's scientific and regulatory reasons for: (1) denying clearance of a 510(k) notification; (2) approving a PMA application; or (3) denying an IDE application. After receiving a denial notification, the recipient may request a supervisory review of the decision. This request must be made no later than 30 days after receipt of the denial notice. The Secretary of HHS is mandated to follow a specific timeframe to review the decision – except in cases that require outside expert consultation.

Section 611

This section explains that notices altering regulation or policy – including notice letters to industry – are deemed guidance documents. These documents are subject to the FDA's good guidance practice rules.

Section 612

This section grants the Secretary of HHS authority to group certain, new devices (without predicates) into Class I or Class II. The Secretary can do so without first issuing a formal determination that the devices are not substantially equivalent, if that device meets certain risk classification criteria.

Section 613

This section expands the current prohibition on profit exemption to encompass not only devices that have been given Humanitarian Device Exemptions, but also to include devices designed to treat or diagnose diseases and conditions that do not occur in pediatric patients. These device exemptions occur in instances where the device's development is deemed impossible, highly impractical, or unsafe.

Section 614

This section reauthorizes 510(k) third party review accreditation as well as third party inspections of factory, warehouse, and manufacturing or processing facilities.

Section 615

This section mandates the Secretary of HHS withdraw its "Guidance for Industry and FDA Staff – 510(k) Device Modification: Deciding When to Submit a 510(k) for a Change to an Existing Device" issued on July 27, 2011. This action is necessary due to the agency's admission that unintended consequences may result by moving forward to implement this guidance. The Secretary of HHS must give stakeholders sufficient opportunity to comment before any future guidance document is made final.

Section 616

This section instructs the FDA to form an advisory committee, comprised of outside stakeholders, to offer recommendations regarding mobile medical applications. The FDA is then directed to issue a report to Congress outlining a proposed strategy and recommendations to design an appropriate regulatory framework to implement health information technology software, including mobile medical applications. This section prohibits the FDA from issuing final guidance on mobile medical applications until it issues its mandated report to Congress.

Title VII – Drug Supply Chain

Section 701

This section expands the information required from registrants who manufacture, prepare, propagate, compound, or process drugs. Specifically, each registrant must provide each facility's unique identifier, point-of-contact email address, as well as specific information about each importer that takes physical possession of a drug.

Section 702

This section requires foreign facilities that manufacture, prepare, propagate, compound, or process drugs to register. The section does so by deeming drugs from an unregistered facility as misbranded. The section also updates registration requirements – mandating a unique facility identifier and point-of-contact email address, as well as similar information on each drug importer and the importer's facilities.

Section 703

This section expands the required product listing to include information on drug recipient establishments. This includes providing a unique facility identifier and point-of-contact email address.

Section 704

This section mandates the Secretary of HHS set up a unique facility identifier system. It also requires the Secretary maintain an electronic database. Finally, the Secretary must guarantee the accuracy and coordination of FDA databases in an effort to identify and inform risk-based inspections.

Section 705

This section directs the Secretary of HHS to carry out drug facility inspections according to a risk-based schedule. The Secretary is not authorized to distinguish between prescription and nonprescription drug products.

Section 706

This section instructs manufacturers to submit certain inspection records (at the Secretary of HHS' request) in a timely and reasonable manner. The submissions are done at the manufacturer's expense. The Secretary must clearly describe what records and information the agency is requesting and provide the manufacturer a confirmation receipt.

Section 707

This section authorizes the Secretary of Homeland Security, at the specific request of the Secretary of HHS, to bar a drug from entering the United States if the product is manufactured in a facility that refused to permit HHS inspections.

Section 708

This section protects drug-related information acquired by the Secretary of HHS from disclosure under the Freedom of Information Act. The authority applies when a federal, state, local, or foreign government agency has requested the information remain confidential. In certain cases, however, the Secretary can reveal drug-related trade secret information via written agreement with the foreign government, as long as the Secretary has certified that HHS is able to protect full trade secret disclosure.

Section 709

This section clarifies criteria to determining a drug has been adulterated. The section says that "current good manufacturing practices" must include manufacturing quality controls and assure raw material safety.

Section 710

This section requires the Secretary of HHS establish an accreditation system. This system must include the recognition of accreditation bodies, the development of model standards, the ability for third party auditors to conduct safety and quality audits used to certify good manufacturing practice compliance, and other purposes. The Secretary must use the audit results to set the drug

risk-based inspection schedule. Finally, this section allows the Secretary to revoke third-party auditor accreditation – including that of foreign governments.

Section 711

This section allows the Secretary of HHS to require electronic submission of certain information by a drug importer as a condition to grant entry. This data includes regulatory status, facility information (unique identifier), and inspection and compliance information.

Section 712

This section authorizes the Secretary of HHS to require establishments that manufacture, prepare, propagate, compound, or process drugs – as well as wholesale distributors – to notify the agency if: (1) there is a substantial loss or theft of a drug; (2) the drug has been or is currently being counterfeited; (3) the counterfeited product has been introduced to the U.S. marketplace; and (4) the counterfeit drug is offered for import to the United States.

Section 713

This section increases the penalty and fine for any person who knowingly and intentionally contaminates a drug when doing so has a reasonable expectation to cause serious, adverse health consequences or death. The penalty is not more than 20 years imprisonment, a fine not to exceed $1 million, or both.

Section 714

This section raises the penalty and fine for any individual who knowingly and intentionally forges or counterfeits drug products. This includes the selling and dispensing of drug products. The penalty is not more than 20 years imprisonment, a fine not to exceed $4 million, or both.

Section 715

This section provides explicit extraterritorial federal jurisdiction over a violation of the Federal Food, Drug and Cosmetic Act so that U.S. authorities can hold people violating the Act accountable.

Section 716

This section requires the courts and administrative agencies to apply Title VII of S. 3187 in a consistent manner with international agreements to which the U.S. is party.

Title VIII – Generating Antibiotic Incentives Now

Section 801

This section offers incentives to develop new qualified infectious disease products (QIDPs). This section provides an additional five year market exclusivity period – in addition to other

exclusivity periods for which the product might qualify. It also clearly defines QIDPs as antibacterial or antifungal drugs intended to treat serious or life-threatening infections.

Section 802

This section makes QIDPs eligible for priority review.

Section 803

This section makes QIDPs eligible for fast track review.

Section 804

This section requires the Government Accountability Office (GAO) to conduct a study outlining the need for QIDP incentives as well as an assessment of QIDP regulatory, review, and development issues.

Section 805

This section mandates the Secretary of HHS to review and, when needed, update clinical trial guidance documents for antibacterial and antifungal drug products. This section also allows the Secretary, upon written request by a sponsor-seeking QIDP approval, to provide clinical trial recommendations.

Section 806

This section directs the Secretary of HHS to submit a report to Congress outlining a comprehensive QIDP strategy and implementation plan. A later requirement mandates the Secretary provide the number of QIDPs, a list of QIDPs – as well as QIDP submissions, approvals, and review times.

Title IX – Drug Approval and Patient Access

Section 901

This section contains a sense of Congress that FDA should help expedite the availability of drugs intended to treat serious or life-threatening diseases and conditions while maintaining safety and effectiveness standards. This section also requires the Secretary of HHS facilitate development and expedite review of "fast-track" products. These are drugs demonstrating potential to meet an unmet need for a serious or life-threatening medical condition.

Section 902

This section requires the Secretary of HHS expedite the development and review of "breakthrough therapy" drugs. In order to be classified as a breakthrough therapy, a drug must treat a serious or life-threatening disease, and preliminary clinical evidence must show that that the drug is a significant improvement over existing therapies.

Section 903

This section mandates the Secretary of HHS to offer consultation opportunities with stakeholder groups from the rare disease community. The Secretary must maintain a list of outside scientific and medical experts to consult on rare disease projects.

Section 904

This section instructs the Architectural and Transportation Barriers Compliance Board to convene a stakeholder working group. This group must develop best practices to help people who are blind or visually impaired access information about prescription drug labels.

Section 905

This section directs the Secretary of HHS to include risk-benefit analysis into its regulatory decision making process.

Section 906

This section authorizes the Secretary of HHS to contract with the National Academies to study how a prize award might incentivize medical product development and innovation.

Section 907

This section reauthorizes the Orphan Product Grants Program through 2017. This program encourages the development of drug, device, biologic, and medical food products to treat rare diseases or conditions.

Title X – Drug Shortages

Section 1001

This section changes current drug shortage manufacturer notification requirements. This section requires all manufacturers of certain drug products to notify the federal government of a permanent discontinuance or a manufacturing interruption that may lead to supply disruptions.

This section further authorizes the Secretary to expedite establishment inspections and application reviews that could mitigate or prevent a drug shortage event. Finally, it mandates the Secretary improve communication, recordkeeping, and regulatory review to determine impact on drug shortages.

Title XI – Other Provisions

Section 1101

This section reauthorizes a sponsor’s ability to obtain separate approval and exclusivity for drugs containing a single enantiomer, when the racemic drug has already been approved.

Section 1102

This section reauthorizes the Critical Path Public-Private Partnerships through fiscal year 2017. The partnership provides funds for industry, the FDA, and academia to work on emerging challenges for medical product development such as biomarkers.

Section 1111 through Section 1113

These sections streamline and modernize regulation of core medical gases. These gases include oxygen, nitrogen, nitrous oxide, carbon dioxide, helium, carbon monoxide, and medical air.

Section 1121

This section changes FDA conflict of interest rules. Congress established conflict of interest rules in the 2007 PDUFA reauthorization. These rules increased advisory committee vacancy rates, especially for committees studying rare diseases. By eliminating the cap on the number of conflict of interest waivers the Secretary of HHS can grant, FDA advisory committees will have greater access to scientific experts. This section retains disclosure provisions outlined in current law, makes annual waiver reporting requirements public, and mandates the agency produce a guidance document should a proposed committee member appear to have a conflict of interest.

Section 1122

This section directs the Secretary of HHS to issue guidance explaining FDA policy when promoting FDA-regulated medical products using the internet. This includes social media outlets.

Section 1123

This section mandates electronic submission of drug, generic drug, biologic, and biosimilar new drug applications after the Secretary of HHS issues a final guidance.

Section 1124

This section instructs the Secretary of HHS to issue a report to Congress outlining federal initiatives to combat prescription drug abuse and misuse. The report must include recommendations identifying opportunities to better utilize federal data sources, distribute best practices, and develop education tools.

Section 1125

This section requires the Secretary of HHS, within 18 months of enactment, to issue tanning bed labeling requirements.

Section 1126

This section requires the FDA work collaboratively with peer regulators to reduce pre-market approval study duplication. This section does not change pre-market standards to review medical products. It directs the FDA to accept data from clinical investigations conducted outside the U.S. if the applicant demonstrates that the data is adequate to meet U.S. standards. The FDA must provide notice to the sponsor if the data is not adequate to support a U.S. application.

Section 1127

This section directs the FDA establish a comprehensive strategy and implementation plan to advance regulatory science. The FDA must, each year from fiscal years 2013 to 2017, report on regulatory science goals. Additionally, the GAO must provide independent assessments on the FDA regulatory science initiative's progress.

Section 1128

This section instructs the FDA to issue a report outlining a comprehensive information technology strategy plan. This plan must be consistent with GAO recommendations. GAO must also report on the FDA's progress in meeting goals outlined in the plan.

Section 1129

This section expands the FDA's annual reporting requirements. This section is specific to medical products covered by the user fee agreements.

Section 1130

This section mandates the Secretary of HHS submit to Congress an integrated management strategy. This management strategy must be based on GAO recommendations. It also must identify goals for the FDA Center for Drug Evaluation and Research; Center for Biologics Evaluation and Research; and Center for Devices and Radiological Health. Finally, this section assigns the GAO to issue a report assessing how well these groups achieve identified goals and objectives.

Section 1131

This section clarifies that risk management and evaluation strategy elements cannot be used to bar supply of a drug to a drug developer when the developer's goal is to begin necessary testing to support a generic drug application.

Section 1132

This section directs the Secretary of HHS to develop and implement strategies soliciting patient views and perspectives during the medical product development process as well as during regulatory discussions.

Administration Position

As of May 16, 2011, the Obama Administration has yet to issue a Statement of Administration Policy.

Cost

The Congressional Budget Office (CBO) released a cost estimate of S. 2516, the bill reported by the Senate HELP Committee, on May 7, 2012. CBO estimates that enacting S. 2516 would:

- Reduce direct spending, on net, by $71 million over the 2013-2017 period and by $358 million over the 2013-2022 period.

- Increase federal revenues, on net, by $5 million over the 2013-2022 period.

CBO has not released a cost estimate for S. 3187.

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